P3-103 NSCLC: Molecular Targeted Therapy Posters, Wed, Sept 5 – Thurs, Sept 6

Evaluation of Epidermal Growth Factor Receptor Mutation Status in Serum DNA as a Predictor of Response to Gefitinib (IRESSA)

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In a previous study, we showed that *EGFR* mutation status in serum DNA was useful as a predictor of response to gefitinib (IRESSA). The aim of this study was to assess the feasibility of detecting EGFR mutations in serum DNA and to evaluate the usefulness of *EGFR* mutation status in serum DNA as a means of predicting a benefit from gefitinib therapy in Japanese patients with NSCLC. We obtained pairs of tumor and serum samples from 42 patients treated with gefitinib and examined them for *EGFR* mutations. *EGFR* mutation status was determined by a direct sequencing method and by Scorpion Amplification Refractory Mutation System (ARMS) technology. *EGFR* mutations were detected in the tumor samples of eight patients and in the serum samples of seven patients. *EGFR* mutation status in the tumors and serum samples was consistent in 39 (92.9%) of the 42 pairs. *EGFR!* mutations were more frequent in women and non-smokers, and there were strong correlations between both *EGFR* mutation status in the tumor samples and serum samples, and objective response to gefitinib ($p<0.001$, Fisher's exact test). Median progression-free survival time was significantly longer in the patients with *EGFR* mutations than in the patients without *EGFR* mutations (194 vs. 55 days, $P=0.016$, in tumor samples; 174 vs. 58 days, $P=0.044$, in serum samples, Log-rank test). Median survival time was longer in the patients with *EGFR* mutations detected by either of the two methods than in the patients without *EGFR* mutations, but the difference was not statistically significant. The results suggest that it is feasible to use serum DNA to detect *EGFR* mutations, and that it's potential as a predictor of response to, and survival on gefitinib is worthy of further evaluation.

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Epidermal growth factor receptor (EGFR) gene mutational status and response to gefitinib in patients with non-small cell lung cancer: A prospective study

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Background: Somatic EGFR gene mutations are reported to be associated with clinical responses to gefitinib and erlotinib in patients with non-small cell lung cancer (NSCLC). Retrospective studies have shown around 75% response rate in patients with tumors that have EGFR gene mutations compared with a response rate of less than 10% in those with wild-type EGFR. We prospectively examined the status of EGFR gene mutations in patients with NSCLC and their response to treatment with gefitinib.

Methods: Clinical samples (formalin-fixed paraffin-embedded tumor tissue, pleural effusion, and sputum) were obtained with informed consent from patients with advanced NSCLC at Toranomon Hospital, and were examined for EGFR mutations by direct sequencing or the peptide nucleic acid-locked nucleic acid PCR clamp method (Cancer Res. 2005;65:7276). Patients who received gefitinib therapy after examining EGFR mutations were then evaluated for their response to gefitinib according to RECIST criteria.

Results: Tumor samples from 60 patients who were enrolled in the study from June 2006 to January 2007 were analyzed. EGFR mutations were detected in 17 of 60 patients (28.3%) (13 females/4 males; 16 never-smokers/ 1 former-smoker; all adenocarcinomas). Detected mutations included 9- to 18-base deletion in exon 19 in 12 patients (70.6%), L858R in exon 21 in 4 (23.5%) and an 18-base insertion in exon 19 in 1 (5.9%), respectively. Ten of 17 patients with EGFR mutations were given gefitinib 250 mg daily (median age: 67 years; 9 females/1 male; all never-smokers; performance status 0-1/2-4=6/4; stage IIIB/IV/postoperative recurrence=2/3/5). Four patients were treated with gefitinib as the first-line therapy. Nine patients had measurable lesions, and the response to gefitinib was PR in four patients, SD in three, and PD in two, respectively. The response rate and disease control rate were 44.4% and 77.8%, respectively. On the other hand, four of 43 patients with wild-type EGFR received gefitinib, but none of these patients achieved CR or PR. No significant adverse events (>grade 3) including acute lung injury/interstitial pneumonia were observed.

Conclusion: EGFR mutations were found in the tumors of 28% of Japanese patients with NSCLC. The disease control rate of gefitinib therapy was extremely good in those who had EGFR mutations. Thus, routine evaluation for the EGFR mutation status is desirable in patients with NSCLC before treatment of gefitinib.

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Response to erlotinib in the neoadjuvant setting for early stage non-small cell lung cancer (NSCLC): a case report

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Background: Erlotinib as single agent is associated with objective response rates of about 12% in unselected patients with NSCLC stage IIIB/IV. Much higher response rates were observed in selected groups of patients selected on the basis of EGFR mutations. To investigate whether erlotinib is able to make an extra contribution to surgical treatment of early stage NSCLC, a phase II study was initiated in the Netherlands. This study is meant to provide a proof of principle if erlotinib is a worthwhile induction therapy option and if erlotinib may be advised as induction regimen for a selected group of patients. We report a remarkable response in one of our first patients.

Case Presentation: A 58-year old woman presenting with a clinical stage I adenocarcinoma in the right upper lobe was asked to participate in the study. After written informed consent, she received erlotinib for